

Claims parent

US 6,686,395 B2

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-continued

| example No. | structure | MS (ES+): m/c = |
|----------------|-----------|--------------------|
| 18ai | | 494 |

Pharmacological Investigations

Kv1.5 channels from humans were expressed in *Xenopus oocytes*. For this, *oocytes* from *Xenopus laevis* were first isolated and defolliculated. RNA encoding Kv1.5 synthesized *in vitro* was then injected into these *oocytes*. After Kv1.5 protein expression for 1–7 days, Kv1.5 currents were measured on the *oocytes* using the two-microelectrode voltage clamp technique. The Kv1.5 channels were in this case as a rule activated using voltage jumps to 0 mV and 40 mV lasting 500 ms. The bath was rinsed with a solution of the following composition: NaCl 96 mM, KCl 2 mM, CaCl₂ 1.8 mM, MgCl₂ 1 mM, HEPES 5 mM (titrated with NaOH to pH 7.4). These experiments were carried out at room temperature. The following were employed for data acquisition and analysis: Geneclamp amplifier (Axon Instruments, Foster City, USA) and MacLab D/A converter and software (AD Instruments, Castle Hill, Australia). The substances according to the invention were tested by adding them in different concentrations to the bath solution. The effects of the substances were calculated as the percentage inhibition of the Kv1.5 control current which was obtained when no substance was added to the solution. The data were then extrapolated using the Hill equation in order to determine the inhibitory concentration IC₅₀ for the respective substances.

The following IC_{50} values were determined in this way for the compounds listed below:

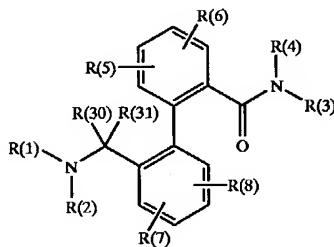
| example No. | IC ₅₀ [μM] |
|-------------|-----------------------|-------------|-----------------------|-------------|-----------------------|-------------|-----------------------|
| 1 a | 6.1 | 2 a | 2.6 | 4 a | 4.1 | 6 b | 3.0 |
| 1 b | 3.3 | 2 b | 0.8 | 4 c | 1.4 | 7 a | -6.0 |
| 1 d | 1.0 | 2 c | 0.7 | 4 d | 1.8 | 8 a | 0.3 |
| 1 e | 0.5 | 2 d | 1.7 | 4 g | 3.4 | 8 b | 0.9 |
| 1 f | 0.4 | 2 e | 3.4 | 4 h | 1.8 | 8 d | 6.4 |
| 1 g | 0.4 | 2 f | 7.1 | 4 i | 4.7 | 8 j | 4.5 |
| 1 h | 4.3 | 2 g | 3.3 | 4 j | 7.1 | 8 k | 3.1 |
| 1 i | 1.7 | 2 h | 2.5 | 4 k | 2.2 | 8 l | 3.5 |
| 1 j | 0.2 | 2 i | 3.3 | 4 l | 0.8 | 8 m | 5.2 |
| 1 k | 2.4 | 2 j | 2.5 | 5 a | 4.5 | 8 n | 3.7 |
| 1 l | 1.4 | 2 k | 3.8 | 5 c | 7.8 | 8 o | 8.4 |
| 1 m | 0.7 | 2 m | 2.6 | 5 d | 1.9 | 8 p | 1.4 |
| 1 n | 1.4 | 3 d | 1.7 | 5 e | 7.2 | 8 q | 7.3 |
| 1 o | 4.4 | 3 k | 2.4 | 6 a | 4.4 | 8 r | 1.0 |
| 1 r | 0.8 | 3 l | 2.6 | 6 b | 1.8 | 8 s | 1.0 |
| 1 s | 1.7 | 3 p | 1.9 | 6 c | 2.5 | 8 x | 3.3 |
| 1 t | 1.3 | 3 r | 1.5 | 6 d | 3.1 | 8 y | 2.8 |
| 1 u | 0.8 | 3 | 3.0 | 6 e | 3.6 | 8 z | 1.6 |
| 8 aa | 0.8 | 8 ab | 1.2 | 8 ac | 1.1 | 9 b | 3.0 |
| 9 c | 2.0 | 9 f | 2.2 | 9 g | 2.2 | 11 a | 2.3 |

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| example No. | IC ₅₀ [μM] |
|-------------|-----------------------|-------------|-----------------------|-------------|-----------------------|-------------|-----------------------|
| 11 b | 7.3 | 11 d | 3.3 | 11 g | 7.8 | 11 h | 5.8 |
| 11 l | 2.7 | 11 m | 3.3 | 11 n | 5.9 | 11 o | 4.4 |
| 11 p | 7.3 | 12 c | 11.2 | 12 f | 11.3 | 12 g | 9.1 |
| 12 h | 4.8 | 12 l | 10.3 | 12 m | 7.7 | 13 b | ~3.0 |
| 13 c | 1.4 | 13 d | 0.5 | 13 e | 2.8 | 13 f | 3.4 |
| 13 g | 1.1 | 13 h | 1.4 | 13 i | 1.2 | 14 a | 3.6 |
| 14 b | 2.7 | 14 d | 2.0 | 14 e | 0.8 | 14 f | 2.5 |
| 15 b | 3.1 | 16 b | 5.2 | 18 a | 7.2 | 18 b | 0.4 |
| 18 c | 4.2 | 18 d | 0.4 | 18 e | 1.7 | 18 f | 1.3 |
| 18 g | 3.9 | 18 h | 0.8 | 18 i | 0.4 | 18 j | 0.7 |
| 18 k | 3.0 | 18 m | 2.1 | 18 n | 0.4 | 18 o | 3.6 |
| 18 p | 4.7 | 18 q | 3.2 | 18 r | 0.7 | 18 s | 0.9 |
| 18 u | 1.1 | 18 v | 0.4 | 18 w | 5.4 | 18 x | 4.6 |
| 17 d | 1.3 | 17 e | 1.8 | 17 c | 2.1 | 18 y | 1.9 |
| 18 z | 1.2 | 18 aa | 0.4 | 18 ab | 1.1 | 18 ac | 10 |
| 18 ad | 0.3 | 18 af | 5.8 | 18 ah | 2.1 | 18 ai | 6.6 |

We claim:

1. A compound of the formula I,



in which:

R(1) is $\text{SO}_2\text{R}(10)$ or $\text{COR}(11)$;

R(10) and R(11) are, independently of one another, defined as R(9);

R(9) is C_xH_{2x} —R(14);

x is 0, 1, 2, 3 or 4

R(14) is cycloalkyl

carbon atoms phenyl, naphthyl or biphenylyl, where phenyl, naphthyl and biphenylyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3 , OCF_3 , NO_2 , CN, COMe , CONH_2 , COME , NH_2 , OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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R(2) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF_3 ;
 R(3) is C_yH_{2y} —R(16);
 y is 0, 1, 2, 3 or 4;
 R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 carbon atoms, phenyl or naphthyl, where phenyl and naphthyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3 , OCF_3 , NO_2 , CN, COOMe , CONH_2 , COMe , NH_2 , OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
 R(4) is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or CF_3 ;
 R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, I, CF_3 , NO_2 , CN, COOMe , CONH_2 , COMe , NH_2 , OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino; and
 R(30) and R(31) independently of one another are hydrogen or alkyl having 1, 2 or 3 carbon atoms; or a pharmaceutically acceptable salt thereof.

2. A compound as claimed in claim 1, in which

R(1) is $\text{SO}_2\text{R}(10)$ or $\text{COR}(11)$;
 R(9) is C_xH_{2x} —R(14);
 x is 0, 1, 2, 3 or 4;
 R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl, where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF_3 , OCF_3 , NO₂, CN, COOMe , CONH_2 , COMe , NH_2 , OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;
 R(2) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF_3 ;
 R(3) is C_yH_{2y} —R(16);
 y is 0, 1, 2, 3 or 4;
 R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF_3 , OCF_3 , CN, COOMe , CONH_2 , COMe , NH_2 , OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
 R(4) is hydrogen or alkyl having 1 or 2 carbon atoms;
 R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF_3 , CN, COOMe , CONH_2 , COMe , NH_2 , OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino; and
 R(30) and R(31) independently of one another are hydrogen or methyl.

4. A compound as claimed in claim 3, in which:

R(1) is $\text{SO}_2\text{R}(10)$ or $\text{COR}(11)$;
 R(9) is C_xH_{2x} —R(14);
 x is 0, 1, 2 or 3;
 R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3 , OCF_3 , OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

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3. A compound as claimed in claim 2, in which:

R(1) is $\text{SO}_2\text{R}(10)$ or $\text{COR}(11)$;
 R(9) is C_xH_{2x} —R(14);
 x is 0, 1, 2, 3 or 4;
 R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF_3 , OCF_3 , CN, COOMe , CONH_2 , COMe , NH_2 , OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
 R(3) is C_yH_{2y} —R(16);
 y is 0, 1, 2, 3 or 4;
 R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF_3 , OCF_3 , CN, COOMe , CONH_2 , COMe , NH_2 , OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4) is hydrogen or alkyl having 1 or 2 carbon atoms;
 R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF_3 , CN, COOMe , CONH_2 , COMe , NH_2 , OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino; and
 R(30) and R(31) independently of one another are hydrogen or methyl.

5. A compound as claimed in claim 4, in which:

R(1) is $\text{COR}(11)$;
 R(9) is C_xH_{2x} —R(14);

x is 0, 1, 2 or 3;
R(14) is cycloalkyl having 5 or 6 carbon atoms or phenyl,
where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;
R(2) is hydrogen;
R(3) is C_xH_{2x}—R(16);
y is 0, 1 or 2;
R(16) is cycloalkyl having 5 or 6 carbon atoms or phenyl
where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;
R(4) is hydrogen; and
R(5), R(6), R(7) and R(8)
independently of one another are hydrogen, F, CF₃, alkyl having 1, 2 or 3 carbon atoms or alkoxy having 1 or 2 carbon atoms; and
R(30) and R(31)
are hydrogen.
6. A pharmaceutical composition, comprising an effective amount of at least one compound as claimed in claim 1 together with a pharmaceutically acceptable vehicle or additive.
7. A method for the therapy of a K⁺ channel-mediated illness, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
8. A method for the therapy of a cardiac arrhythmia which can be eliminated by action potential prolongation, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
9. A method for the therapy of a re-entry arrhythmia, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
10. A method for the therapy of a supraventricular arrhythmia, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
11. A method for the therapy of atrial fibrillation or atrial flutter, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
12. A method for terminating existing atrial fibrillation or flutter to restore sinus rhythm, which comprises administering to a host in need of the termination an effective amount of a compound as claimed in claim 1.
13. A compound as claimed in claim 1, in which:
R(1) is SO₂R(10) or COR(11);
R(9) is C_xH_{2x}—R(14);
x is 0, 1, 2, 3 or 4;
R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl,
where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
R(3) is C_yH_{2y}—R(16);

y is 0, 1, 2, 3 or 4;
R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl,
where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
R(4) is hydrogen or alkyl having 1 or 2 carbon atoms;
R(5), R(6), R(7) and R(8)
independently of one another are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino; and
R(30) and R(31)
independently of one another are hydrogen or methyl.
14. A compound as claimed in claim 1, in which
R(30) and R(31) are both hydrogen;
R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 carbon atoms, phenyl, naphthyl or biphenyl,
where phenyl, naphthyl and biphenyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 carbon atoms, phenyl or naphthyl,
where phenyl and naphthyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.
15. A compound as claimed in claim 2, in which
R(30) and R(31) are both hydrogen;
R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl,
where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl,
where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.
16. A compound as claimed in claim 3, in which:
R(30) and R(31) are both hydrogen;
R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl,
where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F,

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Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.

17. A compound as claimed in claim 4, in which:

R(30) and R(31) are both hydrogen;

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(16) is cycloalkyl having 5 or 6 carbon atoms or phenyl,

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where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms.

18. A compound as claimed in claim 5, in which:

R(14) is cycloalkyl having 5 or 6 carbon atoms or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(16) is cycloalkyl having 5 or 6 carbon atoms or phenyl where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F,

Cl, CF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms.

19. A method for preventing the re-occurrence of arrhythmias, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.

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Claims

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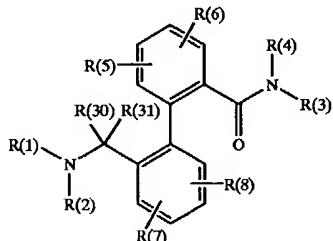
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The following IC_{50} values were determined in this way for the compounds listed below:

| example No. | IC_{50} [μM] | example No. | IC_{50} [μM] | example No. | IC_{50} [μM] | example No. | IC_{50} [μM] |
|-------------|-----------------------|-------------|-----------------------|-------------|-----------------------|-------------|-----------------------|
| 1a | 6.1 | 2a | 2.6 | 4a | 4.1 | 6h | 3.0 |
| 1b | 3.3 | 2b | 0.8 | 4c | 1.4 | 7a | ~6.0 |
| 1d | 1.0 | 2c | 0.7 | 4d | 1.8 | 8a | 0.3 |
| 1e | 0.5 | 2d | 1.7 | 4g | 3.4 | 8b | 0.9 |
| 1f | 0.4 | 2e | 3.4 | 4h | 1.8 | 8d | 6.4 |
| 1g | 0.4 | 2f | 7.1 | 4i | 4.7 | 8j | 4.5 |
| 1h | 4.3 | 2g | 3.3 | 4j | 7.1 | 8k | 3.1 |
| 1i | 1.7 | 2h | 2.5 | 4k | 2.2 | 8l | 3.5 |
| 1j | 0.2 | 2i | 3.3 | 4l | 0.8 | 8m | 5.2 |
| 1k | 2.4 | 2j | 2.5 | 5a | 4.5 | 8n | 3.7 |
| 1l | 1.4 | 2k | 3.8 | 5c | 7.8 | 8o | 8.4 |
| 1m | 0.7 | 2m | 2.6 | 5d | 1.9 | 8p | 1.4 |
| 1n | 1.4 | 3d | 1.7 | 5e | 7.2 | 8q | 7.3 |
| 1o | 4.4 | 3k | 2.4 | 6a | 4.4 | 8r | 1.0 |
| 1r | 0.8 | 3l | 2.6 | 6b | 1.8 | 8s | 1.0 |
| 1s | 1.7 | 3p | 1.9 | 6c | 2.5 | 8x | 3.3 |
| 1t | 1.3 | 3r | 1.5 | 6d | 3.1 | 8y | 2.8 |
| 1u | 0.8 | 3 | 3.0 | 6e | 3.6 | 8z | 1.6 |
| 8aa | 0.8 | 8ab | 1.2 | 8ac | 1.1 | 9b | 3.0 |
| 9c | 2.0 | 9f | 2.2 | 9g | 2.2 | 11a | 2.3 |
| 11b | 7.3 | 11d | 3.3 | 11g | 7.8 | 11h | 5.8 |
| 11l | 2.7 | 11m | 3.3 | 11n | 5.9 | 11o | 4.4 |
| 11p | 7.3 | 12c | 11.2 | 12f | 11.3 | 12g | 9.1 |
| 12h | 4.8 | 12l | 10.3 | 12m | 7.7 | 13b | ~3.0 |
| 13c | 1.4 | 13d | 0.5 | 13e | 2.8 | 13f | 3.4 |
| 13g | 1.1 | 13h | 1.4 | 13i | 1.2 | 14a | 3.6 |
| 14b | 2.7 | 14d | 2.0 | 14e | 0.8 | 14f | 2.5 |
| 15b | 3.1 | 16b | 5.2 | 18a | 7.2 | 18b | 0.4 |
| 18c | 4.2 | 18d | 0.4 | 18e | 1.7 | 18f | 1.3 |
| 18g | 3.9 | 18h | 0.8 | 18i | 0.4 | 18j | 0.7 |
| 18k | 3.0 | 18m | 2.1 | 18n | 0.4 | 18o | 3.6 |
| 18p | 4.7 | 18q | 3.2 | 18r | 0.7 | 18s | 0.9 |
| 18u | 1.1 | 18v | 0.4 | 18w | 5.4 | 18x | 4.6 |
| 17d | 1.3 | 17e | 1.8 | 17c | 2.1 | 18y | 1.9 |
| 18z | 1.2 | 18aa | 0.4 | 18ab | 1.1 | 18ac | 10 |
| 18ad | 0.3 | 18af | 5.8 | 18ah | 2.1 | 18ai | 6.6 |

We claim:

1. A compound of the formula I,



in which:

R(1) is $C(O)OR(9)$, $SO_2R(10)$, $COR(11)$, $C(O)NR(12)R(13)$ or $C(S)NR(12)R(13)$;

R(9) is $C_xH_{2x}-R(14)$;

x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is $OR(15)$ or SO_2Me ;

R(14) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11

carbon atoms, CF_3 , C_2F_5 , C_3F_7 , CH_2F , CHF_2 ,

$OR(15)$, SO_2Me , phenyl, naphthyl or biphenyl,

where phenyl, naphthyl and biphenyl are unsub-

stituted or substituted by 1, 2 or 3 substituents

selected from the group consisting of F, Cl, Br, I,

CF_3 , OCF_3 , NO_2 , CN, $COOMe$, $CONH_2$, $COMe$,

NH_2 , OH, alkyl having 1, 2, 3 or 4 carbon atoms,

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alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF_3 or phenyl which is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3 , NO_2 , CN, $COOMe$, $CONH_2$, $COMe$, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(10), R(11) and R(12) independently of one another are defined as R(9);

R(13) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF_3 ;

R(2) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF_3 ;

R(3) is $C_yH_{2y}-R(16)$; y is 0, 1, 2, 3 or 4, where y cannot be 0 if R(16) is $OR(17)$ or SO_2Me ;

R(16) is $OR(17)$ or a six membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3 , OCF_3 , NO_2 , CN, $COOMe$, $CONH_2$, $COMe$, NH_2 , OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3 , OCF_3 , NO_2 , CN, $COOMe$, $CONH_2$, $COMe$, NH_2 , OH, alkyl having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; or

R(3) is $CHR(18)R(19)$;

R(18) is $C_xH_{2x}-R(16)$, where R(16) is defined as indicated above;

z is 0, 1, 2 or 3;

R(19) is $COOH$, $CONH_2$, $CONR(20)R(21)$, $COOR(22)$, or CH_2OH ;

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, $C_xH_{2x}-CF_3$ or $C_xH_{2x}-phenyl$, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3 , OCF_3 , NO_2 , CN, $COOMe$, $CONH_2$, $COMe$, NH_2 , OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3;

w is 0, 1, 2 or 3;

R(21) is hydrogen or alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(22) is alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(4) is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or CF_3 ;

R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, I, CF_3 , NO_2 , CN, $COOMe$, $CONH_2$, $COMe$, NH_2 , OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms,

dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;

R(30) and R(31) independently of one another are hydrogen or alkyl having 1, 2 or 3 carbon atoms; or

R(30) and R(31) together form a chain of 2 methylene groups;

or a pharmaceutically acceptable salt thereof.

2. A compound as claimed in claim 1, in which

R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12)

R(13);

R(9) is C_xH_{2x}—R(14);

x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is OR(15);

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, C₂F₅, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF₃ or phenyl, which is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(10), R(11) and R(12) independently of one another are defined as R(9);

R(13) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF₃;

R(2) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF₃;

R(3) is C_yH_{2y}—R(16);

y is 0, 1, 2, 3 or 4, where y cannot be 0 if R(16) is OR(17);

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3-, or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; or

R(3) is CHR(18)R(19);

R(18) is C_zH_{2z}—R(16), where R(16) is defined as indicated in claim 1 above;

z is 0, 1, 2 or 3;

R(19) is CONH₂, CONR(20)R(21), COOR(22), CH₂OH;

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C_wH_{2w}—CF₃ or C_wH_{2w}-phenyl, where the

phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3;

w is 0, 1, 2 or 3;

R(21) is hydrogen or alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(22) is alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(4) is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or CF₃; and

R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;

R(30) and R(31) independently of one another are hydrogen or alkyl having 1, 2 or 3 carbon atoms; or

R(30) and R(31) together form a chain of 2 methylene groups.

3. A compound as claimed in claim 2, in which:

R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12)

R(13);

R(9) is C_xH_{2x}—R(14);

x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is OR(15);

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1 or 2 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF₃ or phenyl, which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(10), R(11) and R(12) independently of one another are defined as R(9);

R(13) is hydrogen;

R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

R(3) is CHR(18)R(19);

R(18) is C_zH_{2z}—R(16);

z is 0, 1, 2 or 3;

R(19) is CONH₂, CONR(20)R(21), COOR(22) or CH₂OH;

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C_wH_{2w}—CF₃ or C_wH_{2w}-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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v is 0, 1, 2 or 3;
w is 0, 1, 2 or 3;
R(21) is hydrogen or alkyl having 1, 2, 3, 4 or 5 carbon atoms;
R(22) is alkyl having 1, 2, 3, 4 or 5 carbon atoms; 5
R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, 10 CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; 15
R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, 20 CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
R(4) is hydrogen or alkyl having 1 or 2 carbon atoms; and 25
R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;
R(30) and R(31) independently of one another are hydrogen or methyl; 30
R(30) and R(31) together form a chain of 2 methylene groups.
4. A compound as claimed in claim 2, in which: 35
R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12) R(13);
R(9) is C_xH_{2x}—R(14);
x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is OR(15); 40
R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, 45 CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
R(15) is alkyl having 1 or 2 carbon atoms, 50 cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF₃ or phenyl, which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 55 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
R(10), R(11) and R(12) independently of one another are defined as R(9); 60
R(13) is hydrogen;
R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
R(3) is C_yH_{2y}—R(16);
y is 0, 1, 2, 3 or 4, where y cannot be 0 if R(16) is OR(17); 65
R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom,

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where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; 15
R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; 20
R(4) is hydrogen or alkyl having 1 or 2 carbon atoms;
R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;
R(30) and R(31) independently of one another are hydrogen or methyl; or 25
R(30) and R(31) together form a chain of 2 methylene groups.
5. A compound as claimed in claim 4, in which:
R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12) R(13);
R(9) is C_xH_{2x}—R(14);
x is 0, 1, 2 or 3;
R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃ or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, 30 CF₃, OCF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;
R(10), R(11) and R(12) independently of one another are defined as R(9);
R(13) is hydrogen;
R(2) is hydrogen;
R(3) is C_yH_{2y}—R(16);
y is 0, 1 or 2;
R(16) is pyridyl, where pyridyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms; 35
R(4) is hydrogen; and
R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, CF₃, CN, COOMe, CONH₂, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms or alkoxy having 1 or 2 carbon atoms;
R(30) and R(31) independently of one another are hydrogen or methyl; or 40
R(30) and R(31) together form a chain of 2 methylene groups.
6. A compound as claimed in claim 5, in which:
R(1) is C(O)OR(9) or COR(11);
R(9) is C_xH_{2x}—R(14);
x is 0, 1, 2 or 3;
R(14) is cycloalkyl having 5 or 6 carbon atoms or phenyl, where phenyl is unsubstituted or substi

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tuted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(11) is defined as R(9);
R(2) is hydrogen;
R(3) is C_yH_{2y}—R(16);
y is 0, 1 or 2;
R(16) is pyridyl where pyridyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(4) is hydrogen; and
R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, CF₃, alkyl having 1, 2 or 3 carbon atoms or alkoxy having 1 or 2 carbon atoms;

R(30) and R(31) are hydrogen.

7. A pharmaceutical composition, comprising an effective amount of at least one compound as claimed in claim 1 together with a pharmaceutically acceptable vehicle or additive.

8. A pharmaceutical composition as claimed in claim 7, which further comprises one or more other pharmacologically active compounds.

9. A method for the therapy of a K⁺ channel-mediated illness, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.

10. A method for the therapy of a cardiac arrhythmia which can be eliminated by action potential prolongation, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.

11. A method for the therapy of a re-entry arrhythmia, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.

12. A method for the therapy of a supraventricular arrhythmia, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.

13. A method for the therapy of atrial fibrillation or atrial flutter, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.

14. A method for terminating existing atrial fibrillation or flutter to restore sinus rhythm, which comprises administering to a host in need of the termination an effective amount of a compound as claimed in claim 1.

15. A pharmaceutical composition as claimed in claim 7, which further comprises an effective amount of an IK_r channel blocker.

16. A pharmaceutical composition as claimed in claim 7, which further comprises an effective amount of an IK_s channel blocker.

17. A pharmaceutical composition as claimed in claim 7, which further comprises an effective amount of a beta-blocker.

18. A compound as claimed in claim 1, in which:

R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12) R(13);
R(9) is C_xH_{2x}—R(14);
x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is OR(15);
R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is

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unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1 or 2 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF₃ or phenyl, which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(10), R(11) and R(12) independently of one another are defined as R(9);

R(13) is hydrogen;

R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

R(3) is CHR(18)R(19);
R(18) is C_zH_{2z}—R(16);
z is 0, 1, 2 or 3;

R(19) is CONH₂, CONR(20)R(21), COOR(22) or CH₂OH;

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C_vH_{2v}—CF₃ or C_wH_{2w}-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3;

w is 0, 1, 2 or 3;

R(21) is hydrogen or alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(22) is alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4) is hydrogen or alkyl having 1 or 2 carbon atoms; and R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;

R(30) and R(31) independently of one another are hydrogen or methyl; or

R(30) and R(31) together form a chain of 2 methylene groups.

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19. A compound as claimed in claim 1, in which:

R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12)

R(13);

R(9) is C_xH_{2x}—R(14);

x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is 5 OR(15);

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, 10 cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; 15

R(15) is alkyl having 1 or 2 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF₃ or phenyl, which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, 20 COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(10), R(11) and R(12) independently of one another 25 are defined as R(9);

R(13) is hydrogen;

R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

R(3) is C_yH_{2y}—R(16);

y is 0, 1, 2, 3 or 4, where y cannot be 0 if R(16) is 30 OR(17);

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, 35 where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; 40

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; 45

R(4) is hydrogen or alkyl having 1 or 2 carbon atoms; 50

R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino; 55

R(30) and R(31) independently of one another are hydrogen or methyl; or

R(30) and R(31) together form a chain of 2 methylene groups.

20. A compound as claimed in claim 1, in which 60

R(30) and R(31) are both hydrogen;

R(14) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 carbon atoms, CF₃, C₂F₅, C₃F₇, CH₂F, CHF₂, OR(15), SO₂Me, phenyl, naphthyl or biphenyl, where phenyl, 65 naphthyl and biphenyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group

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consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOME, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOME, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOME, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; and

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C_vH_{2v}—CF₃ or C_wH_{2w}-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOME, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; v is 0, 1, 2 or 3; w is 0, 1, 2 or 3.

21. A compound as claimed in claim 2, in which

R(30) and R(31) are both hydrogen;

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, C₂F₅, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOME, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOME, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3-, or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOME, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; and

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C_vH_{2v}—CF₃ or C_wH_{2w}-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOME, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3;
w is 0, 1, 2 or 3.
22. A compound as claimed in claim 3, in which

R(30) and R(31) are both hydrogen;

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C_vH_{2v}—CF₃ or C_wH_{2w}—phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3;
w is 0, 1, 2 or 3;

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; and

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.

23. A compound as claimed in claim 4, in which

R(30) and R(31) are both hydrogen;

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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ing of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.

24. A compound as claimed in claim 5, in which

R(30) and R(31) are both hydrogen;

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃ or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms; and

R(16) is pyridyl, where pyridyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms.

25. A compound as claimed in claim 6, in which

R(14) is cycloalkyl having 5 or 6 carbon atoms or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms; and

R(16) is pyridyl where pyridyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms.

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